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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,434	04/14/2000	CORNELIA BERGHOF	2727-100J	1917

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EXAMINER	
SOUAYA, JEHANNE E	
ART UNIT	PAPER NUMBER
1634	15

DATE MAILED: 05/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/485,434	Applicant(s) BERGHOF ET AL.
	Examiner Jehanne Souaya	Art Unit 1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,10-14,16-18,20-22,24-26 and 28-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,10-14,16-18,20-22,24-26 and 28-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Please note that the art unit designation for the examiner has changed from 1655 to 1634.

1. Currently, claims 7, 10-14, 16-18, 20-22, 24-26, and newly added claims 28-48 are pending in the instant application. All the amendments, declaration and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are either newly applied or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claim 16 is objected to because it fails to end in a period. Appropriate correction is required.

Maintained Rejections

Claim Rejections - 35 USC § 112

Indefinite

4. Claims 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 13 is indefinite in the recitation of "have been replaced by analogous building blocks known per se as probes or primers" as it is unclear if the 1 or 2 nucleotides have been replaced by probes or primers. It is further unclear what is meant by the term analogous building blocks as it is unclear what the claim considers "analogous" to the nucleotides that are being replaced.

B) Claim 14 is indefinite with respect to the term "nucleic acid-like" as it is unclear what characteristics the modified groups can possess such that they remain "nucleic-acid-like".

Response to Arguments

The response asserts that claims 13 and 14 are canceled, however the amendment does not authorize cancellation of these claims.

Written Description

5. Claims 7, 10-14, 16-18, 20-22, 24-26, and newly added claims 28-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Firstly, it is unclear from the recitation in the claim whether the nucleic acids in question can possess a sequence of more than one of the specific SEQ ID NOS recited in the claims. Furthermore, the amendment to claim 7 encompasses any nucleic acid sequence comprising a sequence that is shorter than SEQ ID NO 1-10 or to sequences that are larger than SEQ ID NOS

1-10 (the latter also applies to newly added or amended claims 18, 36-39 and 48). The claim as amended thus reads on a sequence "comprising" (open terminology) a shortened sequence compared to SEQ ID NO 1-10. In other words, any sequence that is larger than SEQ ID NOS 1-10, are encompassed by the claims as presently amended. Additionally, claims 7, 10-14, 16-18, 20-22, 24-26 and newly added claims 28-35, and 40-47 read even more broadly on sequences that are larger than SEQ ID NOS 1-10, wherein the nucleic acid need only possess 8 or 9 out of 10 contiguous nucleotides of the nucleic acid sequence of SEQ ID NOS 1-10. The claims are further drawn to methods of using such nucleic acids as well as kits comprising such nucleic acids. The specification, however, only teaches the specific nucleic acid sequences of SEQ ID NOS 1-10. The claimed sequences, however, read on a large number of sequences that will detect specific subspecies of Salmonella. With respect to claim 13, the claims read on any sequence such that 20% of it's nucleotides can be modified in each string of 10 successive nucleotides. Such a claim would read on a sequence only having 60% complementarity to SEQ ID NOS 1-10.

Furthermore, amendment of claim 7 to -a nucleic acid *consisting* of...-, does not overcome the rejection as the claim would still read on a broad genus of sequences that have not been described in the specification. For example, the molecule of SEQ ID NO 1 consists of 20 nucleotides. Claim 7, however, stipulates that a nucleic acid molecule need only possess 80% identical sequences out of 10 contiguous nucleotides of SEQ ID NO 1. Such a molecule could differ from SEQ ID NO 1 in 11 out of 20 positions, thus encompassing a molecule which could

read on a probe or primer for a large number of other genes or sequences, from any species of Salmonella, which have not been described in the specification. The same analysis holds for claims 10-14, 16-18, 20-22, 24-26 and newly added claims 28-35, and 40-47.

The claimed invention represents a broad genus for which a representative number of species of such a genus must be disclosed to fulfill the description requirement of 112, first paragraph. As set forth by the Court in *Vas Cath Inc. V. Mahurkar,* 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date, applicant was in possession of the claimed invention. Absent a written description disclosing a representative number of the species of the isolated nucleic acids of SEQ ID NOS 1-10, or to methods of using such a broad genus of nucleotides, the specification fails to show that applicant was, in fact, "in possession of the claimed invention" at the time the application for patent was filed.

Response to Arguments

The response traverses the rejection. The response cites *In re Edwards*,568 F.2d 1349 (C.C.P.A. 1970) as the lead case on the written description requirement. The response further asserts that determining whether the written description requirement is satisfied requires reading the disclosure in light of the knowledge possessed by the skilled artisan. These arguments have been thoroughly reviewed but were found unpersuasive as the claims still encompass sequences from genomic DNA of different Salmonella species and serovars or strains. It is further noted, that the claims are sufficiently broad as to encompass sequences from unknown serovars or

strains of Salmonella. With regard to the citation of *In re Edwards* these arguments have been thoroughly reviewed but were found unpersuasive. Firstly, the written description guidelines applied by the examiner are based on the *Regents of the University of California v. Eli Lilly* decision in 1997 which is directed to nucleic acids, whereas the CCPA decision in *In re Edwards* was in 1970. Secondly, the examiner has not required that the specification must outline each and every sequence encompassed by the claims, but a representative number of the species encompassed by the broadly claimed genus. The disclosed structural feature: a nucleic acid molecule of SEQ ID NO 1-10 or a nucleic acid molecule comprising 10 contiguous nucleotides within SEQ ID NOS 1-10, does not constitute a substantial portion of the claimed genus of sequences from any species, strain, or isolate of Salmonella. One of skill in the art, would not be able to envision the detailed chemical structure of the encompassed nucleic acid molecules, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, the polynucleotide itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

For these reasons and the reasons made of record above, and in previous office actions, the rejection is maintained.

Claim Rejections - 35 USC § 103

6. Claims 7, 10-14, 16-18, 20-22, 24-26, and newly added claims 28-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes et al (WO95/00664).

The claims are drawn to isolated nucleic acid molecules that can distinguish between the following *Salmonella enterica* subspecies: *enterica, salamae, arizonae, diarizonae, houtenai, bongori*, and *indica*. The nucleic acid molecules are characterized in that the sequences of each subspecies have been aligned to determine regions of similarity and variability to design primers and probes that universally hybridize to a number of subspecies and specifically hybridize to a certain subspecies and not to other subspecies, thereby identifying nucleic acid samples as containing *Salmonella enterica* and further distinguishing each subspecies through PCR amplification or hybridization.

Holmes teaches an invention which provides nucleic acid molecules for the detection and identification of *Salmonella* species, and for detecting one or more *Salmonella* serotypes and to kits comprising these nucleic acid molecules (see abstract). Holmes teaches a need for detecting

Salmonella because the incidence of salmonellosis has increased significantly during the last two decades in western countries and that while standard culture methods are still widely used for detection of *Salmonella* in foods, the control of infection depends on the availability of rapid and precise tests for monitoring of primary animal production (see p. 1). Holmes teaches that nucleic acid based methods for detection of a DNA or RNA from a target organism have proliferated and that the invention of Holmes is based on using certain fragments of the *Salmonella typhimurium* LT2 chromosome (or corresponding nucleic acid fragments having the same sequence of bases, including RNA, PNA, etc) as primers in PCR and other amplification systems, in particular certain fragments corresponding to regions of the genome which are highly conserved in *Salmonella* species (see paragraph bridging pages 2 and 3). Holmes further teaches that fragments to conserved regions are useful in detecting and identifying *Salmonella* species generally, while fragments from less conserved regions are useful for identifying infections from different serotypes of *Salmonella* (see p. 3). Holmes teaches using 146 *Salmonella* strains (table 2) and 82 non *Salmonella Enterobacteriaceae* strains (table 3). Holmes further teaches that 8 oligonucleotide sequences were selected from the sequence and tested for their ability to discriminate between *Salmonella* and non *Salmonella* bacteria and teaches various results in the primer pairs ability to identify and distinguish *Salmonella* form non *Salmonella* bacteria and form different serotypes of *Salmonella* (see p. 14, 15, and table 1,2 and 3, examples 1 and 2). Holmes specifically teaches evaluation of a *Salmonella* specific PCR assay and the detection of *enterica, salamae, arizonae, diarizonae, houtenai, bongori,* and *indica* and teaches application of

the general method in the detection of *Salmonella* in pork and beef (example 3). Holmes teaches kits containing these nucleic acid primers and probes for use in the method taught by Holmes. It is also noted that the sequences of SEQ ID NOS 1, 3, 6, and 9 are found in SEQ ID NO 1, taught by Holmes.

Although Holmes does not teach the exact nucleic acid molecules "consisting" of the SEQ ID Nos taught in claim 7, Holmes (for example) provide motivation for the skilled artisan to construct the sequences of claim 7 and the sequences encompassed by the broadly claimed invention. Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to construct sequences as Holmes teaches how to construct nucleic acid molecules for the purpose of detecting different serotypes of *Salmonella*. The ordinary artisan would have been motivated to construct such nucleic acid molecules as Holmes teaches a need for the detection and differentiation of *Salmonella* for the purposes of controlling infection caused by *Salmonella*.

It should be noted that the state of the art was very high at the time the invention was filed to construct probes and primers for the detection and differentiation of different strains of closely related bacteria and fungi. For example, a number of US patents were given to Hogan et al (5,714,321 is enclosed) to methods and nucleic acids for detecting and differentiating different strains of bacteria. A large number of references were available, at the time the invention was made, that taught the ordinary artisan how to align sequences of bacteria to determine regions of similarity and variability to detect and differentiate different strains of bacteria. As the strains

and subspecies of the bacteria were known and available in the art at the time of filing, it would have been prima facie obvious to one of ordinary skill to align the sequences of different subspecies of *Salmonella* for the purpose of providing nucleic acids for detecting and differentiating different subspecies of *Salmonella*.

Response to Arguments

The response traverses the rejection. The response asserts that Holmes does not teach a using a specific combination of SEQ ID NOS 1-10, or SEQ ID NOS 1-2 and 6-10, or SEQ ID NOS 3-10. This argument has been thoroughly reviewed but was found unpersuasive as none of the claims are directed to such specific combinations. None of the claims are specifically drawn to a specific set of nucleic acid molecules. Instead, the claims recite the SEQ ID NOS in Markush format such that any combination, even different combinations of a single SEQ ID NO, are encompassed by the claim.

The response further asserts that it is well settled that there must be some prior art teaching which would provide the necessary incentive or motivation for modifying the reference teachings. This argument was thoroughly reviewed but was found unpersuasive. From the teaching of Holmes, the ordinary artisan would have been taught how to construct probes and primers by aligning sequences from different species of Salmonella, for the purposes of obtaining probes and primers for the detection of specific species of Salmonella. The ordinary artisan would have considered such probes and primers to be equivalent to the sequences taught by Holmes for the purposes of detection of specific species of Salmonella, absent evidence to the

contrary. The response further asserts that "obvious to try" is not a standard under 35 USC 103. This argument has been thoroughly reviewed because Holmes teaches a high expectation of success that designing primers and probes for the detection of specific species of Salmonella can be achieved. Applicant's cite areas in the Holmes reference where teachings of false positives and false negatives are taught, however Holmes also teaches that primers ST3, ST4, ST5, and ST7 gave no false positive reactions at different wash temperatures (see p. 14, lines 1-3). Furthermore, table 1 discloses that ST4 and ST5 gave no false negatives at 55 and 59 deg C. Therefore, contrary to the assertions of the response, a reasonable expectation of success is taught in the prior art.

The response further asserts that the Declaration clearly demonstrates that the specific combination of SEQ ID NOS 1-2 and 6-10 allows specific detection of all 560 strains of Salmonella tested. The declaration has been thoroughly reviewed. It is unclear, however, how the teachings of the declaration provide unexpected findings over the teachings of Holmes as Holmes teaches a specific set of oligonucleotides that gave no false positive or false negative results. Furthermore, were the declaration or the specification found to teach unexpected results, for the declaration or the teachings in the specification to overcome the rejection of the claims under 35 USC 103(a), the claims would have to be commensurate in scope with the unexpected results, in this case, the specific combination of nucleic acids "consisting" of SEQ ID NOS 1-2, 6-9 and 10 and at specific hybridization and wash temperatures (see MPEP 716.02(d)). As presently amended, none of the claims are drawn to such. Furthermore, the claims as written

encompass sequences which need only possess 80% identity or 8 or 9 out of 10 nucleotides identical to 10 contiguous nucleotides of one of the recited SEQ ID NOS. These claim limitations are sufficiently broad that the claims are not commensurate in scope with the teachings in the specification. For these reasons and the reasons made of record in previous office actions, the rejection is maintained.

New Grounds of Rejection

7. Claims 7, 10-14, 22, 24-26, and newly added claims 28-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 7, 28, and 32, are indefinite in the recitation of "allows the detection of ..." as it is unclear if the nucleic acid molecule detects Salmonella or whether it is capable of such, but does not necessarily. This rejection can be overcome by reciting instead --wherein the nucleic acid sequence detects all representative..."

B) Claim 18 is indefinite as it is unclear how the kit of claim 48 is used to detect the presence or absence of bacteria.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. No claims are allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya
Patent examiner
Art Unit 1634
5/2/02

W. Gary Jones
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